ORGANIC LETTERS

2000
Vol. 2, No. 5
625−627

Synthesis of 2-Oxazolidinones by Direct Palladium-Catalyzed Oxidative Carbonylation of 2-Amino-1-alkanols

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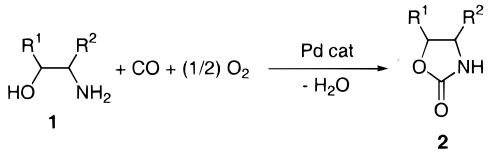
Received December 21, 1999

ABSTRACT

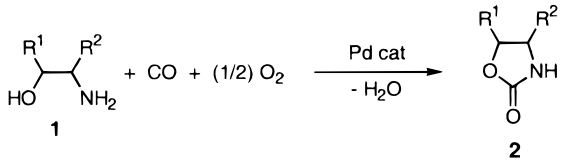


1 2

2-Oxazolidinones 2 are obtained in excellent yields (up to 100%) and with unprecedented catalytic efficiencies (up to 2000 mol of product/mol of catalyst used) by direct PdI_2/KI-catalyzed oxidative carbonylation of the readily available 2-amino-1-alkanols 1. Reactions are carried out in MeOH as the solvent at 100 °C using a 1/6/5 CO/O_2/air mixture (60 atm total pressure at 25 °C).

2-Oxazolidinones **2** are a very important class of heterocyclic compounds. Chiral 2-oxazolidinones are widely used as chiral auxiliaries in many important asymmetric syntheses,[1] and some molecules containing the 2-oxazolidinone moiety have shown antibacterial activity.[2] Recently, they have also found application as intermediates in the synthesis of aldehydes[3] and chiral amines.[4]

2-Oxazolidinones are usually prepared by reaction of 2-amino-1-alkanols **1** with diethyl carbonate.[5] We wish to report herein the preparation of **2** by direct palladium-catalyzed oxidative carbonylation of **1** according to eq 1.[6]



1 2 (1)

Our method consists of the reaction of **1** at 100 °C with carbon monoxide and oxygen (CO/O_2/air = 1/6/5, 60 atm total at 25 °C) in MeOH as the solvent in the presence of PdI_2 in conjunction with an excess of KI (200 mol/mol of PdI_2). The use of pure oxygen rather than oxygen diluted with air invariably led to lower yields of **2**, probably due to competitive oxidation processes.

Table 1 reports the results obtained with different β-amino alcohols. 2-Oxazolidinones **2** were consistently obtained in excellent yields (86−100%) and with unprecedented catalytic efficiencies for this kind of reaction (860−2000 mol of

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10.1021/ol9913789 CCC: $19.00
Published on Web 02/12/2000

Table 1. Synthesis of 2-Oxazolidinones **2** by PdI_2/KI-Catalyzed Oxidative Carbonylation of 2-Amino-1-alkanols **1**[a]

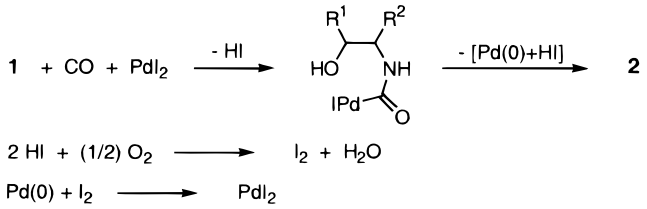
entry	**1**	R^1	R^2	**1**/PdI_2	conversn of **1** (%)[b]	yield of **2** (%)[c]
1	**1a**	H	H	2000	96	90 (85)
2	**1b**[d]	Me	H	2000	100	100 (92)
3[e]	**1b**[d]	Me	H	2000	69	53
4	**1c**[d]	Ph	H	2000	99	87 (79)
5	**1d**[d]	H	Me	2000	97	93 (85)
6	**1e**[f]	H	Ph	2000	100	98 (89)
7	**1f**[g]	H	Me_2CH	2000	79	57
8	**1f**[g]	H	Me_2CH	1000	100	100 (91)
9	**1g**[g]	H	$PhCH_2$	2000	84	65
10	**1g**[g]	H	$PhCH_2$	1000	100	86 (78)

[a] Unless otherwise noted, all reactions were carried out in MeOH (0.5 mmol of **1**/mL of MeOH, 10−15 mmol scale based on **1**) at 100 °C for 15 h under 60 atm of a 1/6/5 mixture of CO/O_2/air in the presence of PdI_2 in conjunction with 200 equiv of KI. [b] Determined by GLC. [c] GLC yield (isolated yield) based on **1**. [d] Racemic. [e] The reaction was carried out using a KI/PdI_2 molar ratio of 100 rather than 200. [f] *R* enantiomer. [g] *S* enantiomer.

product/mol of catalyst used). Although a substrate/catalyst ratio as high as 2000 could be used successfully with most substrates (entries 1, 2, and 4−6), for less reactive 2-amino-1-alkanols such as L-valinol (**1f**) and L-phenylalaninol (**1g**) a substrate/catalyst ratio of 1000 ensured faster kinetics and higher yields of the corresponding 2-oxazolidinones (compare entries 7 and 9 with entries 8 and 10, respectively). The lower yield of **2** obtained with a lower amount of catalyst in such cases suggests the occurrence of a competitive uncatalyzed decomposition pathway of the substrates.

A large excess of both oxygen and iodide anions is essential for the process. In fact, by employing the conditions we previously used for the oxidative carbonylation of 1-alkynes, i.e. KI/PdI_2 molar ratio = 10 under 20 atm total pressure of a 3:1 mixture of CO/air,[7] no reaction at all occurred. Very poor results were also obtained when the reaction was carried out with KI/PdI_2 = 200 when the oxygen partial pressure was only 1−2 atm (as in the mixture CO/air = 3:1 at 20 or 40 atm of total pressure) or using KI/PdI_2 = 10 under an oxygen partial pressure of 35 atm (as in the mixture CO/O_2/air = 1/6/5 at 60 atm of total pressure). On the other hand, the use of a KI/PdI_2 molar ratio of 100 rather than 200 with CO/O_2/air = 1/6/5 (60 atm total pressure) led to less satisfactory results with respect to KI/PdI_2 = 200 (compare entries 2 and 3). We believe that a large excess of iodide anions and oxygen are primarily required to ensure a fast reoxidation of Pd(0) according to Scheme 1 (anionic iodide ligands are omitted for simplicity). As we already suggested,[7] the most likely mechanism of reoxidation of Pd(0) ensuing from the oxidative carbonylation process in our reactions involves the oxidation of HI by oxygen to give iodine, which then oxidatively adds to Pd(0). In the presence of an amino group, HI is almost completely "blocked" as ammonium salt, and the reoxidation process becomes more difficult.[8] However, a large excess of iodide ions may effectively shift the acid−base equilibrium to the left, and a

Scheme 1



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high O_2 partial pressure may further favor the oxidation of HI to iodine, thus allowing fast and effective regeneration of the catalytically active species PdI_2.

Acknowledgment. Financial support from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica is gratefully acknowledged.

Supporting Information Available: Experimental procedures and characterization data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL9913789